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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,018	10/12/2000	Philip Gotwals	A018	6239

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Biogen Inc
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EXAMINER	
ANDRES, JANET L	

ART UNIT	PAPER NUMBER
1646	23

DATE MAILED: 10/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/423,018	GOTWALS ET AL.	
	Examiner	Art Unit	
	Janet L. Andres	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,8,9 and 11-39* is/are pending in the application.

4a) Of the above claim(s) *8,9 and 11-21* is/are withdrawn from consideration.

5)☒ Claim(s) *5* is/are allowed.

6)☒ Claim(s) *22-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 24 July 2003 has been entered. Claims 5, 8, 9, and 11-39 are pending in this application. Claims 8, 9, and 11-21 are withdrawn from consideration as being drawn to a non-elected invention. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Rejoinder

2. This application contains product and process claims (claims 14-21). Applicant has elected claims directed to the product. When Applicant elects product claims and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined

claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim Rejections - 35 USC § 112

3. Claims 22-25 and 27-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for fusion proteins comprising amino acids 1-160 of SEQ ID NO:8 or 9, does not reasonably provide enablement for homologues, equivalents, or variants of these sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant has amended the claims and states that the amendment obviates any conceivable enablement rejection. However, these claims encompass molecules of undefined

(equivalents, variants) or very limited homology (60%) to the disclosed sequences. Applicant has described rabbit and human receptors. However, applicant has not described the characteristics of these proteins so that one of skill in the art could predictably identify other sequences of limited homology that would also bind TGF-β. Applicant has not described the properties or characteristics of the sequences that are required for binding. The amino acid sequence of a polypeptide determines its structural and functional properties, and predictability of which amino acids can be substituted is extremely complex and well outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Further, while recombinant techniques are available, it is not routine in the art to screen large numbers of nucleic acids that might potentially encode such proteins where the expectation of obtaining similar activity is unpredictable. Thus one of skill in the art would require additional guidance, such as information as to what structural features would result in the ability to make a functional fusion protein, in order to practice the invention commensurate with the scope of the claims without undue experimentation.

4. Claim 22-25 and 27-29 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims encompass "native" molecules and "naturally occurring" variants. Such molecules exist in nature and have particular structures. Applicant has not described all such

structures and there is no way to predict what they would be. Thus one of skill in the art would not conclude that Applicant was in possession of "naturally occurring" and "native" molecules.

Claim Rejections - 35 USC § 103

5. Claims 22-26 and 28-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. patent 6,046,157 (Lin et al.) in view of U.S. patent 5,605,690 (Jacobs et al.) for reasons of record in the office actions of paper nos. 14, 18, and 21 and restated below.

The Lin patent teaches a soluble fragment of human TGF-β RII that includes amino acids 1-166 of SEQ ID NO: 8 of the Lin patent (column 9, lines 13-19). Residues 1-160 are identical to residues 1-160 of the instant SEQ ID NO: 9. The Lin patent teaches that this region can be used as a soluble receptor that binds TGF-β. Methods of using such a receptor to bind TGF-β and methods of using such binding to modulate the effects of TGF-β are claimed in claims 1-21. The Lin patent fails to teach fusion proteins. The Jacobs patent teaches fusion proteins with a soluble TNF receptor and IgG1 in column 7, lines 41-58. The Jacobs patent thus teaches fusion of a soluble receptor with a constant region, IgG, IgG1, and sequences comprising hinge domains. The Jacobs patent further teaches improved function due to the resulting bivalency. It would have been obvious to one of ordinary skill in the art to combine the teachings of the Lin patent with those of the Jacob patent to make human TGF-β RII fusion proteins as instantly claimed. One of ordinary skill would have been motivated to do so because the Lin patent teaches that soluble TGF-β RII is useful, and the Jacobs patent teaches a method of improving the usefulness of a soluble receptor. Thus one of ordinary skill would have expected the modification of the Jacobs patent to improve the usefulness of the invention of the Lin patent.

Applicant argues that Lin does not teach fusion proteins and that Jacobs does not teach TGF-βRII. Applicant further argues that "speculating that modulation of TGF-β might have an ameliorative effect on certain diseases" does not equate with Applicant's claimed invention. Applicant further states that Lin does not focus on TGF-βRII. Applicant argues that, based Jacobs and the "unspecified" TGF-βR of Lin, one of ordinary skill would not have expected that TGF-βRII fusion proteins as claimed by Applicant could be used for fibroproliferative disorder. Applicant states that Lin and Jacobs "merely skirt around" the production of fusion proteins and "merely generalize about" TGF-β receptors. Applicant concludes there is no basis to conclude that one of ordinary skill would have used Jacobs as a template to select TGF-βRII from Lin, and that there is no reason to believe that any advantages of polymeric TNF [receptor] would translate to TGF-βRII.

Applicant's arguments have been fully considered but have not been found to be persuasive. Lin does not merely "speculate" or refer to "unspecified" TGF-β receptors. Claims 12-21 of Lin are drawn to methods of altering TGF-β effects in a mammal using soluble human TGF-βRII. The receptor is referred to by both name and SEQ ID number. Thus Lin clearly specifies TGF-βRII. Applicant is also reminded that claims in U.S. patents are considered to be enabled; clearly, one of ordinary skill, on reading the claims of Lin, would expect soluble TGF-βR II to be a useful molecule. It is not necessary that Applicant's precise intended use be contemplated; such an intended use does not alter the nature of the composition, and would regardless be readily apparent to one familiar with the functions of TGF-β. Similarly, Jacobs does not "skirt around" fusion proteins. Jacobs claims in claims 1-6 that such proteins are useful for lowering levels of TNF-α. As stated previously and above, the advantage of the fusion

protein is that it increases the valency - that is, the number of soluble receptors present and able to bind the ligand. That advantage does not depend on the nature of the receptor itself. Thus one of ordinary skill would expect the advantages of fusion proteins to translate to TGF-βRII.

CLAIM 5 IS ALLOWED. CLAIMS 22-39 ARE REJECTED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 872-9306 or (703) 872-9307 for after final communications.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[yvonne.eyler@uspto.gov]**.

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.
October 16, 2003

JANET ANDRES
PATENT EXAMINER